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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)

7230-9

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on _____

Signature _____

Typed or printed name _____

Application Number

10/748,637

Filed

December 30, 2003

First Named Inventor

BRACKETT, N.L.

Art Unit

1651

Examiner

SCHUBERG, L.J.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record. 56,712
Registration number _____

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____



Signature

Nicholas A. Zachariades, Ph.D.

Typed or printed name

561-653-5000

Telephone number

September 25, 2007

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Brackett N. L., et al.

Confirmation No: 6890

Application No.: 10/748,637

Examiner: SCHUBERG, L. J.

Date Filed: December 30, 2003

Group: 1657

For: INCREASING SPERM MOTILITY

Attn: **Mail Stop AF**

Commissioner for Patents

P. O. Box 1450

Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Dear Sir:

In response to the Final Office Action dated June 25, 2007 Applicant respectfully files herewith a Notice of Appeal and requests review of the present application before filing an appeal brief.

Related Appeals

The issues presented in the present application are not related to any pending appeal.

Status of the Claims

Claims 1-9 are pending in the application. Claims 1, 2, 5, 6, 8-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Alexander et al (US 6,180,355 B1). Claims 1, 2, 5, 6, 8-19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 B1) in view of Gruschwitz et al (*Journal of Andrology* 1996) and Angelopoulos et al (*Fertility and Sterility* 1999). Claims 3 and 4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 B1), Gruschwitz et al (*Journal of Andrology* 1996) and Angelopoulos et al (*Fertility and Sterility* 1999) as applied to claims 1, 2, 5, 6, and 8-19 above, and further in view of Brackett et al (*Physical Therapy* 1996).

Clear Errors for Review

Applicants respectfully assert that Alexander et al (US 6,180,355 B1) does not anticipate claims 1, 2, 5, 6, 8-19. The instant invention is directed, in part, to method of increasing motility of sperm, by providing from a subject a biological sample comprising sperm and at least one cytokine; and contacting the biological sample with an agent that inactivates or reduces the biological activity of the at least one cytokine selected from the group consisting of TNF α , IL1 β , and IL6.

The Examiner asserts in the instant Office Action that:

Alexander teaches the use of sandwich ELISA for cytokines in a semen sample (column 11 line 5). The use of antibodies that specifically bind to the cytokines in the semen such as $\text{TNF}\alpha$, $\text{IL1}\beta$, and IL6 is taught (column 11 line 10) (claims 1,5,6,8-15). The subject's condition causes increased cytokine levels in the semen, which inherently impairs fertility (as taught by Applicant page 5 lines 1-5).

Since Alexander is explicitly practicing all the steps of Applicant's method as claimed by administering cytokine antibodies that specifically bind to the claimed cytokines in a semen sample, Alexander anticipates Applicant's claimed method.

Applicants respectfully disagree with the assertions of the Examiner. Applicants have provided the Examiner with 37 C.F.R. § 1.132 declarations from the inventors and from a person of skill in the art (Dr. Dana Ohl) which outline and discuss in detail that the Examiner wrongly interprets Alexander's teaching, i.e., the Examiner assumes that effects on sexual function also occur in fertility. Alexander discusses using generally available techniques of analysis of cytokines to diagnose and treat "Chronic Pelvic Pain Syndrome (CPPS)" or non-bacterial prostatitis. Alexander makes further reference to the symptoms and side effects of CPPS including sexual dysfunction. Alexander makes no reference to infertility, nor is it alleged in Alexander's patent or in the general medical literature that infertility is caused by CPPS. Alexander also discusses systemic therapy, and in no way teaches or discloses the *in vitro* treatment of biological specimens, as taught by Applicants. Further, it is common knowledge in general medicine that infertility and sexual dysfunction are separate entities which should not be confused (See, for example, Dr. Ohl's 37 C.F.R. § 1.132 declaration filed March 29, 2007).

In summary, Alexander discusses cytokines in the semen to diagnose a condition or disease such as CPPS/Chronic Prostatitis. Alexander does not demonstrate or suggest that the administration of the anticytokine agents/antibodies are active in the seminal plasma or bind to the cytokines there. In fact, one of ordinary skill in the art would recognize that they are by example and by intent treating a systemic disease (supposedly autoimmune) which has seminal cytokines as its markers. Since the two conditions are vastly different, Alexander cannot be compared to the instant invention and as such cannot anticipate the instant invention.

Claims 1, 2, 5, 6, 8-19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 B1) in view of Gruschwitz et al (*Journal of Andrology* 1996) and

Angelopoulos et al (*Fertility and Sterility* 1999). Applicants respectfully disagree with the Examiner's assertions that the above-cited references teach, disclose or make obvious the instant invention.

Alexander et al., neither teach or disclose treating the seminal plasma is helpful in treating any disease. In contrast, the instant invention teaches, in part, that elevated cytokines in the seminal plasma cause reduced sperm motility which can be treated in a novel manner, i.e., by neutralizing these cytokines in the seminal plasma. Combining Gruschwitz with Alexander does not result in the instant invention. Gruschwitz discusses a myriad of conflicting data and is directed to urogenital infections which would result in an inflammatory immune response. Thus, the effect of an infection would result in an increase in cytokines. Treating a subject based on Gruschwitz, as alleged by the Examiner, using "Alexander's method as an obvious choice" would not cure one of infertility. Applicants' research has shown no evidence of chronic prostatitis in SCI men, the very subjects from which the semen samples were obtained (Randall et al., *J Urol* 2003:170;897-900). Angelopoulos et al, does not cure the deficiencies of Alexander in view of Gruschwitz. Angelopoulos reported the effects of tissue culture versus addition of pentoxifylline and 2-deoxyadenosine on non-motile sperm in testicular biopsies of azoospermic men.

Angelopoulos further is directed to the occurrence of immotile testicular spermatozoa in testicular biopsies as a physiological event resulting from immaturity or attachment to Sertoli cells – not a pathologic condition. Applicants further provided the declaration of an expert, Dr. D. Ohl, under 37 C.F.R. § 1.132, wherein, Dr. Ohl describes, as one of ordinary skill in the art, that these references do not rise to the level of obviousness. Thus, in contrast to the Examiner's assertions, treating a patient who is infertile with a systemic administration of anticytokine agents of Alexander, in view of Gruschwitz which discusses an anti-inflammatory response in a urogenital infection, and further in view of Angelopoulos which discusses the effects of tissue culture versus addition of pentoxifylline and 2-deoxyadenosine on non-motile sperm in testicular biopsies of azoospermic men, would still not result in the instant invention. That is, the patient would not be treated for infertility nor would the patients fertility be changed by following these references. (See, also for example, the 37 C.F.R. § 1.132 Declarations of record). In contrast to the Examiner's assertions, Applicants have demonstrated causation in that treating seminal plasma *in vitro* with anticytokine agents improves sperm motility in patients with SCI. Therefore, applicants submit that the examiner's assertion that "the cited art provides the requisite teachings and motivation to make and use the claimed method" is incorrect.

Claims 3 and 4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 B1), Gruschwitz et al (Journal of Andrology 1996) and Angelopoulos et al (Fertility and Sterility 1999) as applied to claims 1, 2, 5, 6, and 8-19 above, and further in view of Brackett et al (Physical Therapy 1996).

As discussed above, Alexander discusses a method of treatment by systemically administering agents to the patient directly to treat CPPS. Administration of anticytokine agents is via oral or various injectable routes. In contrast, Applicants treat the seminal plasma and sperm after identifying these cytokines is a novel way of improving sperm motility. Alexander does not teach or disclose elevated cytokines in the seminal plasma cause reduced sperm motility and treatment of the seminal plasma.

Alexander, in view of Gruschwitz, and Angelopoulos are centered around the interpretation of treating a condition “associated with” as discussed by Alexander i.e. neither Alexander, nor Alexander in view of the cited references, teach or disclose infertility treatments. In contrast, Alexander discusses sexual dysfunction due to CPPS. The cited references do not cure any of the deficiencies of Alexander. Applicants submit that one of ordinary skill in the art would realize that this “condition” means systemic illness such as CPPS (or even rheumatoid arthritis) that is indicated or marked by elevated cytokines in the seminal plasma rather than the treatment of the effects of cytokines in the seminal plasma on sperm motility. That is, treatment of sperm with anticytokine agents would not cure CPPS. Further, Brackett *et al.*, does not teach or disclose that sperm may be treated with anticytokine agents to increase sperm motility. Substituting Brackett for Alexander’s systemic treatment of a disease is not an obvious leap to make for one of ordinary skill in the art. For example, Alexander would teach away from directly treating the seminal plasma. There is no teaching as to the amounts, types of antibodies, that motility would be affected etc.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 B), Gruschwitz et al (Journal of Andrology 1996) and Angelopoulos et al (Fertility and Sterility 1999) as applied to claims 1, 2, 5, 6, and 8-19 above, and further in view of Gerris (European Society of Human Reproduction and Embryology 1999).

Alexander et al (US 6,180,355 B), Gruschwitz et al (Journal of Andrology 1996) and Angelopoulos et al have been discussed above. None of these references alone or in view of each other

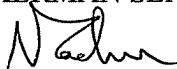
teach or disclose treating male infertility. Each of these references are directed to disease states. Angelopoulos neither teaches or discloses cytokines and sperm motility. Thus, each reference cannot be taken in view of the other as none of these references would even provide an expectation of success of treating male infertility. Nor, do any of these references, alone or in combination provide a motivation to combine these references. Gerris discusses that sperm from the vagina can be retrieved from ICSI. No therapeutic or diagnostic techniques are ascribed to these sperm. Furthermore, the quality of the sperm is most likely to be in a form that would not be advantageous for treating infertility. The Examiner asserts that:

One of ordinary skill in the art would have been motivated to use the method of Alexander to treat semen samples obtained from a woman's reproductive tract because Gerris teaches that this is an excellent alternative for sperm collection for patients who are opposed to masturbation for religious reasons. One of ordinary skill in the art would have had a reasonable expectation of success because this collection method had been used previously for infertility with success (page 213 column 2).

Applicants respectfully disagree with the Examiner's assertions. First, Alexander does not teach or disclose treating infertility. Taking a sperm sample from a vagina, as suggested by the Examiner, and treating a patient who is infertile with systemic administration of anticytokine agents of Alexander, would not change the status of an infertile male to a fertile male as suggested by the Examiner. Thus, neither of these references alone or in combination teach the instant invention.

Accordingly, it is respectfully submitted that the claims are in condition for allowance and clear error has been committed in the final Office Action. The Commissioner is hereby authorized to charge any additional fees which may be required at any time during the prosecution of this application without specific authorization, or credit any overpayment, to Deposit Account Number 50-0951.

Respectfully submitted,
AKERMAN SENTERFITT



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Date: September 25, 2007

Docket No. 7230-9